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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/778,200	02/06/2001	John Kisiday	01997/537001	8784

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CHOATE, HALL & STEWART LLP
EXCHANGE PLACE
53 STATE STREET
BOSTON, MA 02109

EXAMINER	
NAFF, DAVID M	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 06/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/778,200	KISIDAY ET AL.	
	Examiner	Art Unit	
	David M. Naff	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 2/22/05 & 4/13/05.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-8,19,20,22-24 and 27-40 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-8,19,22-24 and 27-40 is/are rejected.

7)☒ Claim(s) 20 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S.O.O.

DETAILED ACTION

Amendments of 2/22/05 and 4/13/05 in response to an office action of 8/17/04 amended claim 30, and added new claims 33-40.

Claims examined on the merits are 1-8, 19, 20, 22-24 and 27-40, which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is unclear as to the meaning and scope of "predetermined compression scheme". It is uncertain as to conditions of compression that will be considered a compression scheme. Moreover, it is uncertain how subjecting to static or dynamic compression in claim 30 is further limited by requiring a predetermined compression scheme since a predetermined compression scheme is inherent when subjecting to static or dynamic compression. One will not subject the scaffold to static or dynamic compression without previously determining how compression is to be applied.

Claim Rejections - 35 USC § 103

Claims 1-3, 5-8, 19, 22-24 and 27-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holmes et al (5,955,343) in view of Hubbell (6,129,761) for the type of reasons set forth in the previous office action of 8/17/04 and for reasons herein.

The claims are drawn to a scaffold containing amphiphilic peptides having alternating hydrophobic and hydrophilic amino acids, which are self-assembled into a beta-sheet to encapsulate cells in the scaffold. In claims 36-39, the scaffold is prepared by methods of incubating the peptides and cells in a solution of osmolarity to not allow the peptides to self-assemble, and adding an electrolyte that initiates the peptides to self-assemble and ecapsulate the cells. Alternatively, the peptides can be first incubated in the solution of required osmolarity, followed by adding the electrolyte.

Holmes et al (col 11, lines 32-35) disclose culturing cells on a membrane or matrix formed by self-assembling of peptides as required by the present claims. The peptides are stable in aqueous solution and self-assemble into a macroscopic structure or matrix when exposed to salt (col 1, lines 32-35). The structures produced can also encapsulate cells since the pore size of the structure is large enough to allow nutrients and products to diffuse, and cells being larger than the pores are contained (col 12, lines 4-9).

Hubbell discloses a scaffold for implanting containing cells encapsulated in a hydrogel (col 5, lines 55-60), and which can contain biologically active agents such as therapeutic agents (col 7, lines

15-21). The hydrogel is produced by forming a polymer solution containing cells and crosslinking the polymer.

Rather than culture the cells on the membrane or matrix of Holmes et al, it would have been obvious to encapsulate the cells in the membrane or matrix as suggested by Hubbell encapsulating cells in a hydrogel for implanting and by Holmes et al disclosing encapsulating cells in the membrane or matrix as an alternative to attaching cells to the membrane or matrix. The membrane or matrix of Holmes et al is inherently a scaffold. The peptides of Holmes et al may be combined with collagen (col 11, lines 26-28), which is an extracellular matrix protein. Chondrocytes disclosed by Hubbell (col 11, line 58) produce extracellular matrix protein, and it would have been obvious to use chondrocytes to produce the collagen disclosed by Holmes et al. The collagen would have inherently resulted in an increase in strength, stiffness and equilibrium compression modulus as required by certain dependent claims. Growth factors as disclosed by Holmes et al (col 11, lines 35-38) would be a chemoattractant as in claim 2. Additionally, the membrane or matrix of Holmes et al may contain a therapeutic compound (col 11, lines 3-11) as in claim 2. The condition of claim 8 will be inherent when encapsulating cells in the membrane or matrix of Holmes et al. Compression that can be within the scope of claims 30, 33 and 40 will not result in a different membrane or matrix than obtained by Holmes et al when encapsulating cells as suggested by Hubbell. Handling the membrane or matrix of Holmes et al will inherently result in applying some compression.

Hubbell discloses molding (col 12, line 22) and would have suggested pre-shaping as in claim 29. Selecting an optimum amount of cells as in claim 31 for a particular function would have been within the skill of the art. Cells encapsulated in the membrane or matrix of Holmes et al will inherently divide as in claim 32 after being placed in a culture medium as suggested by Holmes et al (col 12, lines 1-9). Peptides used by Holmes et al inherently have an adhesion site as in claim 3. The methods of claims 36-39 for producing the scaffold of claim 1 containing encapsulated cells would have been obvious to produce the membrane or matrix of Holmes et al when containing encapsulated cells in view of Holmes et al disclosing that self-assembly of the peptides does not occur until after a salt is added. The salt is an electrolyte, and cells can obviously be combined with the peptides before the salt is added so that self-assembly will occur in the presence of the cells and result in entrapment of the cells in the membrane or matrix. The conditions of claims 34 and 35 will be inherent when encapsulating cells in the membrane or matrix of Holmes et al as set forth above.

Response to Arguments

Applicants urge that Holmes et al does not suggest encapsulating cells in a macroscopic scaffold as claimed. However, Holmes et al is not applied alone, but in combination with Hubbell, and the claimed invention becomes obvious when the references are considered together as a whole rather than each alone. The claims do not exclude a

membrane as a scaffold. The specification at page 24, line 3, Figures 9A and 9C show structures that can be considered a membrane.

While Holmes et al may not explicitly describe how cells can be encapsulated, it is believed how to encapsulate the cells will be obvious to one of ordinary skill in the art when Hubbell is also considered, and suggesting that cells can be encapsulated simply by adding cells to the peptides before self-assembly and allow self-assembly to occur in the presence of the peptides. Self-assembly of the peptides of Holmes et al does not occur until after a salt is added. The solution containing the peptides before the salt is added inherently has an osmolarity to not allow the peptides to self-assemble. Obviously, cells can be combined with the peptides before the salt is added so that self-assembly will occur in the presence of the cells and result in entrapment of the cells in the membrane or matrix. This will be further apparent from Hubbell crosslinking a polymer in presence of cells to encapsulate the cells in a crosslinked polymer. Incubating cells and peptides under conditions that do not allow self-assembly, and then adding an electrolyte to cause the peptides to self-assemble would have been obvious from Holmes et al disclosing that the peptides do not self-assemble in aqueous solution until a salt is added. This procedure would have been an obvious method to use when encapsulating cells as suggested by Holmes et al (col 12, lines 5-10), and is also suggested by Hubbell mixing cells with a polymer solution and then crosslinking the polymer to form a hydrogel. Apparently Holmes et al believed that encapsulated cells in

the self-assembled peptide matrix can survive, or otherwise encapsulating cells would not have been mentioned. There is nothing to suggest that self-assembly of peptides while cells are present will cause cells not to survive. Cells surviving crosslinking of a polymer to form a hydrogel as disclosed by Hubbell would have led one to expect that cells can also survive self-assembly of peptides. The structure of a matrix formed by self-assembly of peptides is not sufficiently different from a matrix formed by crosslinking a polymer to lead one to believe that cells cannot survive in the self-assembled peptide matrix.

Applicants urge that Hubbell teaches away from encapsulating cells in the membrane of Holmes et al. However, Hubbell is not applied alone for suggesting encapsulating cells in the membrane, but is combined with Holmes et al disclosing that cells can be encapsulated in the membrane (col 12, lines 5-9). Holmes et al forming the membrane fast and Hubbell slowly polymerizing does not make unobvious that cells can be encapsulated in the membrane.

The Proceedings of the National Academy of Sciences (1993) (Exhibit A) and Exhibits B, C and D were commented on in the previous office action, and these comments still apply.

Applicants urge that Hubbell was published in 1996 as shown by exhibit B three years after the Holmes et al invention of self-assembly of peptides, and Hubbell does not mention self-assembly of peptides to encapsulate cells. However, this does not make the claimed invention unobvious since Hubbell may not have known about the

Holmes et al invention when the Hubbell application for patent was filed. This also applies to exhibit A showing Holmes et al disclosing self-assembly of peptides before the invention of Hubbell. Holmes et al clearly considered self-assembly of peptides to encapsulate cells to be useful way to encapsulate cells, and it would have been obvious to follow the teachings of Holmes et al without Hubbell disclosing the use of self-assembly of peptides to encapsulate cells.

In regard to exhibit C, the present invention being published in a scientific journal does not establish that the invention is unobvious. There is no evidence establishing that publication depends on the work done being unobvious. The disclosure of exhibit D in regard to the present invention was published after the present application was filed, and cannot render the invention unobvious at the time present application was filed. Furthermore, Hubbell mentioning the invention in exhibit D does not mean that Hubbell considered the invention unobvious. Hubbell makes no statement in regard to being obvious or unobvious. Moreover, such a statement would be a matter of opinion. The exhibit does not state that self-assembled peptides are ECM-like, but rather states that ECM-like material is desirable. In the last paragraph on page 555 of exhibit D, after mentioning reference 91, it is stated that technical hurdles are still to be overcome. This indicates that Hubbell did not consider the present invention to be a final solution to the problem of obtaining an acceptable ECM-like material.

In regard to claim 19, while Holmes et al may envision combining peptides and collagen as asserted by applicants, it would have been obvious when Hubbell is considered that chondrocytes (col 7, line 8) can be the encapsulated cells of Holmes et al, and the function of these cells to produce extracellular matrix protein is well known.

As to arguments concerning claim 30, this claim contains no limitation as to the amount and form of compression applied other than being static or dynamic, and being a predetermined compression scheme, and the claim does not exclude incidental compression resulting from normal handling. Compression being a predetermined scheme does not specify specific compression conditions different than can be incidental. The specification cannot put a limitation in the claim that is not in the claim. Claim limitations can be given their broadest reasonable interpretation. The claim encompasses very small amounts of compression that will not change the scaffold from that without compression, and will not provide the equilibrium compression modulus disclosed in the specification.

Claim Rejections - 35 USC § 103

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1-3, 5-8, 19, 22-24 and 27-40 above, and further in view of Holmes et al (PNAS).

The claim requires cells encapsulated to be neurons.

Holmes et al (PNAS) disclose attaching neurons to a self-assembling peptide scaffold and growing the neurons.

When encapsulating cells in a self-assembling peptide membrane or matrix as set forth above, it would have been obvious to use neurons as the cells to obtain the function of neurons as suggested by Holmes et al (PNAS) attaching neurons to a self-assembling peptide scaffold. Holmes et al (PNAS) further disclose that the peptides self-assemble to form a hydrogel (first page, left col, about line 8).

Response to Arguments

Applicants rely on arguments traversing the above rejection to traverse this rejection. These arguments are unpersuasive for reasons set forth above.

Conclusion

Claim 20 is allowable, but is objected to as being dependent on a rejected claim.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

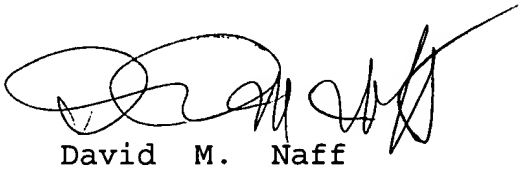
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 751-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David M. Naff
Primary Examiner
Art Unit 1651

DMN
6/21/05